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APPLICATION NO. FILING DATE FIRST NAMED INVENTOR ATTORNEY DOCKET NO. 09/405,499 09/23/99 O'REILLY Y 05213-0640 **EXAMINER** 023594 HM12/0719 JOHN S. PRATT HUFF.S KILPATRICK STOCKTON LLP **ART UNIT** PAPER NUMBER 1100 PEACHTREE SUITE 2800 1642 ATLANTA GA 30309 DATE MAILED: 07/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks** 

	Application No.	Applicant(s)								
Office Action Summers	09/405,499	O'REILLY ET AL.								
Office Action Summary	Examiner	Art Unit								
	Sheela J Huff	1642								
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondenc address								
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.  - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.  - Faillure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).  - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).										
1) Responsive to communication(s) filed on										
	– · s action is non-final.									
3) Since this application is in condition for allowar	nce except for formal matters, pr	osecution as to the ments is								
closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.										
Disposition of Claims  AN  Claim(s) 52 55 57 66 and 68 73 in/ora panding	in the emplication									
	Claim(s) <u>52-55,57-66 and 68-73</u> is/are pending in the application.									
	4a) Of the above claim(s) is/are withdrawn from consideration.									
<u> </u>	5) Claim(s) is/are allowed.									
	6)⊠ Claim(s) <u>52-66 and 68-73</u> is/are rejected.									
7) Claim(s) is/are objected to.										
8) Claim(s) are subject to restriction and/or election requirement.										
Application Papers										
9) The specification is objected to by the Examiner.										
10) ☐ The drawing(s) filed on is/are: a) ☐ accept	•									
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).										
11) ☐ The proposed drawing correction filed on is: a) ☐ approved b) ☐ disapproved by the Examiner.										
If approved, corrected drawings are required in reply to this Office action.										
12) The oath or declaration is objected to by the Exam	miner.	•								
Pri rity under 35 U.S.C. §§ 119 and 120										
13) Acknowledgment is made of a claim for foreign	priority under 35 U.S.C. § 119(a)	-(d) or (f).								
a) ☐ All b) ☐ Some * c) ☐ None of:										
1. Certified copies of the priority documents										
2. Certified copies of the priority documents have been received in Application No										
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).										
* See the attached detailed Office action for a list of the certified copies not received.										
14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).										
<ul> <li>a)           The translation of the foreign language provisional application has been received.</li> <li>15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.</li> </ul>										
Attachment(s)	. <u></u>									
Notice of References Cited (PTO-892)   Notice of Draftsperson's Patent Drawing Review (PTO-948)   Information Disclosure Statement(s) (PTO-1449) Paper No(s)	5) Notice of Informal Pa	(PTO-413) Paper No(s) atent Application (PTO-152)								

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#### **DETAILED ACTION**

### Response to Amendment

1. The amendment filed on 6/21/01 has been considered. Applicant's arguments are deemed to be persuasive-in-part.

Claims 52-55, 57-66 and 68-73 are pending.

- 2. The rejection under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's argument.
- 3. The rejection under 35 U.S.C. 112, first paragraph, is withdrawn in favor of a new one.

# Response to Arguments Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 52-55, 57-66 and 68-73 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7

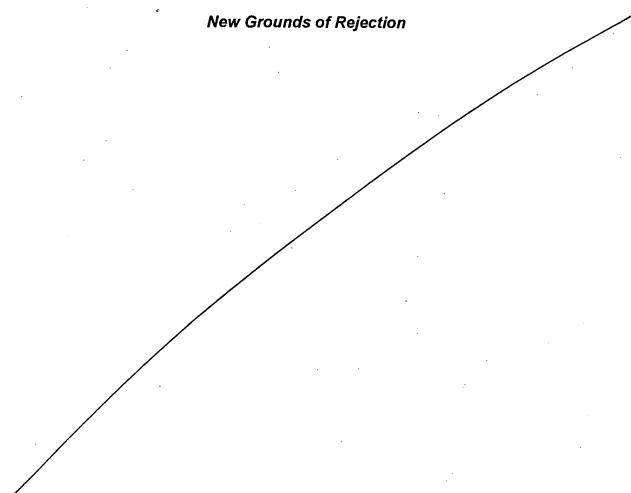
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and 17-23 of U.S. Patent No. 5854205. The reasons for this rejection are of record in paper no. 5, mailed 12/19/00.

Applicant indicates that a terminal disclaimer will be filed.

3. Claims 52-55, 57-66 and 68-73 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 15-17 and 19-20 of copending Application No. 09/315689. The reasons for this rejection are of record in paper no. 5, mailed 12/19/00.

Applicant should note that 09/315689 has been allowed.



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### Claim Rejections - 35 USC § 112

7. Claims 52-55, \$7-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

The claims are directed to an isolated protein <u>comprising</u> a fragment of NC1 wherein the fragment inhibits angiogenesis. This reads on **any** protein comprising NC1 or a fragment thereof. The specification does not support any protein comprising NC1 or a fragment thereof.

Changing "comprising" to -consisting of-will overcome this rejection.

8. Claims 52-55, 57-66 and 68-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for endostatin (as defined by its molecular weight, N-terminal sequence and ability to inhibit endothelial cell proliferation in vitro), does not reasonably provide enablement for a protein comprising or consisting of any fragment of NC1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims encompass a protein that has a portion of the NC1 region. The specification makes it clear that there are specific regions needs for activity and page 44 discloses that longer fragments of the specific region are not active. However, the

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specification provides no guidance as to what are the required elements for activity.

Thus, undue experimentation would be required by one skilled in the art to make and use the instant invention.

9. Claims 52-55, 57-66 and 68-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims, even if "comprising" is changed to --consisting-- read on a NC1 region from any collagen and this NC1 regions from any collagen would be able to inhibit angiogenesis.

Thus, the instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The specification proposes to discover other members of the genus by using structural similarity (ie referring to the fact that all collagens have NC1) and inhibitory activity. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art, at the time of applicant's invention, does not provide compensatory structural or correlative teachings

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sufficient to enable one of skill to isolate and identify the inhibitory molecules encompassed and no identifying characteristic or property of the instant inhibitory molecules is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

There are about 18 collagen molecules that were defined at the time of applicant's earliest priority. While each collagen does have a NC domain, the specification only shows that NC domains containing SEQ ID No. 1 or 2 have antiangiogenic activity. These sequences are found in collagen XVIII, however it is clear that collagen XV has very little homology to SEQ Id No 1 or 2. A sequence search of SEQ. Id No 1 against the database provided no hits. A sequence search of SEQ Id No. 2 against the database showed that collagen XV 42.6% homology (see below).

SUMMARIES										
•										
R	esult		Query							
	No.	Score	Match	Length	DB	ID	Description	Pred. No.		
				· ·						
	1	184	93.4	684	1	CA1H_HUMAN	COLLAGEN ALPHA 1(XVIII			
	2	141	71.6		1	CA1H_MOUSE	COLLAGEN ALPHA 1(XVIII			
	3	84	42.6		1	CA1E_HUMAN	COLLAGEN ALPHA 1(XV) C	7.17e-04		
	4	74	37.6		1	PAFA_CANFA	PLATELET-ACTIVATING FA	6.08e-02		
	5	70	35.5		1	UBS1_YEAST	UBIQUITIN-CONJUGATING	3.27e-01		
	6	68	34.5		1	DPOL_HSV11	DNA POLYMERASE (EC 2.7			
	7	68	34.5	1235	1	DPOL_HSV1K	DNA POLYMERASE (EC 2.7			
	8 9	68	34.5	1235	1	DPOL_HSV1A	DNA POLYMERASE (EC 2.7	7.40e-01		
		68	34.5	1235	1	DPOL_HSV1S	DNA POLYMERASE (EC 2.7	7.40e-01		
	10	67	34.0	586	1	YJS6_YEAST	HYPOTHETICAL 67.3 KD P	1.11e+00		
	11	67	34.0	899	1	ANDR_MOUSE	ANDROGEN RECEPTOR.	1.11e+00		
	12	67	3,4.0	902	1	ANDR_RAT	ANDROGEN RECEPTOR.	1.11e+00		
	13	67	34.0	919	1	ANDR_HUMAN	ANDROGEN RECEPTOR.	1.11e+00		
	14	66	33.5	347	1	Y806_METJA	HYPOTHETICAL PEPTIDASE	1.65e+00		
	15	66	33.5	440	1	YA33_SCHPO	HYPOTHETICAL 49.6 KD P	1.65e+00		
	16	66	33.5	440	1	PAFA_MOUSE	PLATELET-ACTIVATING FA	1.65e+00		
	17	66	33.5	586	1	TALA_POVBO	LARGE T ANTIGEN.	1.65e+00		
	18	66	33.5	595	1	VP1_BPCHP	PROTEIN VP1 (ORF1).	1.65e+00		
	19	66	33.5	647	1	KNRL_DROME	KNIRPS-RELATED PROTEIN	1.65e+00		
	20	65	33.0	441	1	PAFA_HUMAN	PLATELET-ACTIVATING FA	2.45e+00		
	21	65	33.0	622	1	THRB_HUMAN	PROTHROMBIN PRECURSOR	2.45e+00		
	22	65	33.0	709	1	ANDR_RABIT	ANDROGEN RECEPTOR (FRA			
	23	65	33.0	2329	1	YLJ6_CAEEL	HYPOTHETICAL 272.0 KD	2.45e+00		

Thus, one of skill in the art, after looking at applicant's specification and the sequence homology between collagen XV and collagen XVIII (which has SEQ. Id No. 1 or 2) would not readily envision that collagen XV would possess antiangiogenic activity. In fact, a fair and reasonable reading of the sequence searches only shows that collagen I has homology to SEQ ID No. 1 and/or 2. Thus, after a close look at the sequences of the different collagens and at collagen XVIII (which is where SEQ ID No. 1 and 2 were derived), it is clear that the different collagens do not all possess a sequence similar to these. Thus, while each collagen does possess an NC domain, it is clear that not all of them have SEQ ID No. 1 or 2, which is what applicant has shown to inhibit angiogenesis.

## Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
- 10. Claims 52-54, 57-62 are rejected under 35 U.S.C. 102(e) as being anticipated by Olsen et al US 5643783 (filed 12/1/93).

This reference discloses collagen XVIII. It is inherent that the NC1 region in XVIII inhibits angiogenesis.

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### Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is (703) 305-7866. The Examiner can normally be reached on Monday and Thursday from 5:30am to 2:00pm.

If attempts to teach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Tony Caputa, can be reached on (703)308-3995.

The FAX phone number for the group is (703)308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [anthony.caputa@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196. Sheela J. Huff
July 17, 2001

Sheela J. Huff Primary Examiner